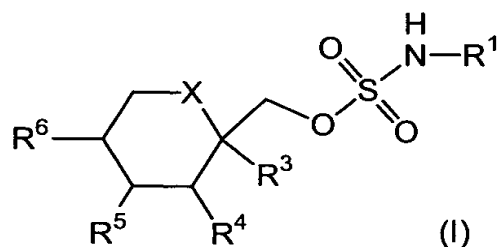


We Claim:

1. A continuous process for the preparation of a compound of formula (I)

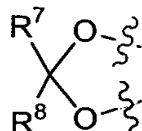


5 wherein

X is selected from CH₂ or O;

R¹ is selected from the group consisting of hydrogen and C₁₋₄alkyl;

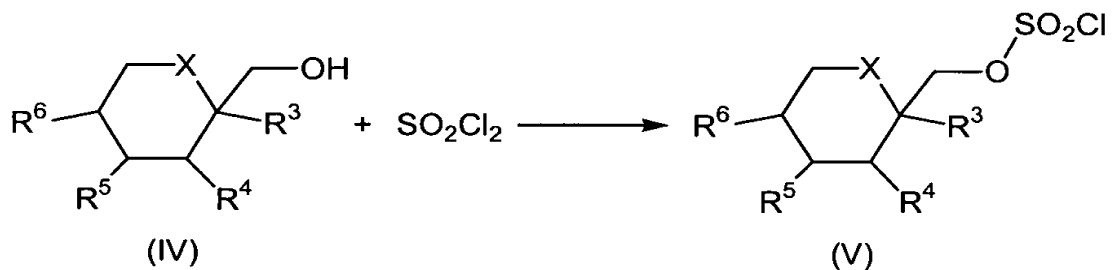
10 R³, R⁴, R⁵ and R⁶ are each independently selected from hydrogen or lower alkyl and, when X is CH₂, R⁵ and R⁶ may be alkene groups joined to form a benzene ring and, when X is O, R³ and R⁴ and/or R⁵ and R⁶ together may be a methylenedioxy group of the formula:



15 wherein

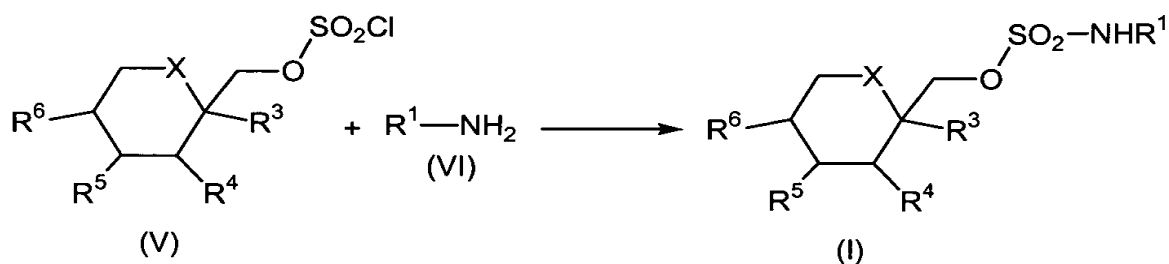
R⁷ and R⁸ are same or different and are hydrogen, lower alkyl or are alkyl and are joined to form a cyclopentyl or cyclohexyl ring;

20 comprising



(A) reacting a suitably substituted compound of formula (IV) with sulfuryl chloride;
 in the presence of an organic or inorganic base;
 in a first organic solvent comprising at least one
 5 solvent selected from a cyclic ether, a straight or
 branched chain dialkyl ether, an aromatic hydrocarbon,
 or a mixture of a cyclic, straight or branched chain
 dialkyl ether and an aromatic hydrocarbon solvent;
 to form the corresponding compound of formula (V);

10



(B) reacting the compound of formula (V) with a
 suitably substituted compound of formula (VI);
 15 in a second organic solvent comprising at least the
 solvent used in step (A);
 to form the corresponding compound of formula (I).

20

2. The process as in Claim 1, wherein the organic or
 inorganic base is an organic base.

3. The process as in Claim 2, wherein the organic base
 is pyridine.

25

4. The process as in Claim 1, wherein the first
 organic solvent comprises at least one solvent selected
 the group consisting of a cyclic ether, a straight or
 branched chain dialkyl ether, an aromatic hydrocarbon

solvent and a mixture of a cyclic, straight or branched chain dialkyl ether and an aromatic hydrocarbon solvent.

5 5. The process as in Claim 4, wherein the first organic solvent comprises a cyclic ether or a straight or branched chain dialkyl ether.

6. The process as in Claim 5, wherein the first organic solvent is glyme.

10 7. The process as in Claim 1, wherein the sulfuryl chloride is present in an amount greater than about 0.9 moles per mole of the compound of formula (IV).

15 8. The process as in Claim 1, wherein the base is present in an amount greater than about 1 molar equivalent of the compound of formula (IV).

20 9. The process as in Claim 8, wherein the molar ratio of the compound of formula (IV) to the base is at least about 1:1.05.

10. The process as in Claim 1, wherein the temperature of the reaction in Step (A) is less than about 50°C.

25 11. The process as in Claim 1, wherein the second organic solvent is glyme.

30 12. The process as in Claim 1, wherein the compound of formula (VI) is present in an amount greater than about 1 molar equivalent of the compound of formula (V).

13. The process as in Claim 12, wherein the molar ratio of the compound of formula (VI) to the compound of formula (V) is at least about 2:1.

5 14. The process as in Claim 1, wherein the compound of formula (VI) is ammonia and the ammonia is fed into the reactor at a pressure of about 19 psia.

10 15. The process as in Claim 1, wherein the temperature of the reaction in Step (B) is in the range of from about -30 to about 50°C.

15 16. The process as in Claim 1, wherein the compound of formula (V) is formed in a solution comprising the compound of formula (V) and the first organic solvent.

20 17. The process as in Claim 16, wherein the sulfonyl chloride is reacted in amount equal to about 1 equivalent relative to the compound of formula (IV), further comprising concentrating the solution comprising the compound of formula (V) and the first organic solvent to remove at least about 20% of the solvent mass..

25 18. The process as in Claim 16, wherein the sulfonyl chloride is reacted in amount greater than about 1 equivalent relative to the compound of formula (IV), further comprising concentrating the solution comprising the compound of formula (V) and the first organic
30 solvent to remove at least 70% of the solvent mass.

19. The process as in Claim 16, further comprising concentrating the solution comprising the compound of formula (V) and the first organic solvent to an oil.

5 20. The process as in Claim 16, further comprising treating the solution comprising the compound of formula (V) and the first organic solvent to remove volatiles.

10 21. The process as in Claim 1, wherein step (A) and step (B) are each run in a continuous stirred tank reactor.

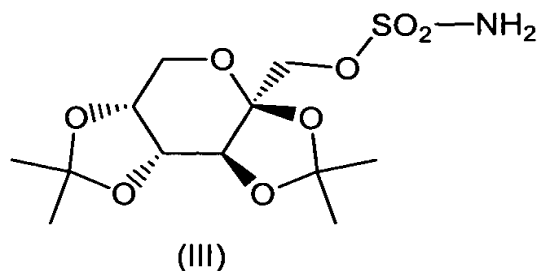
22. A compound prepared according to the process of Claim 1.

15 23. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the compound of Claim 22.

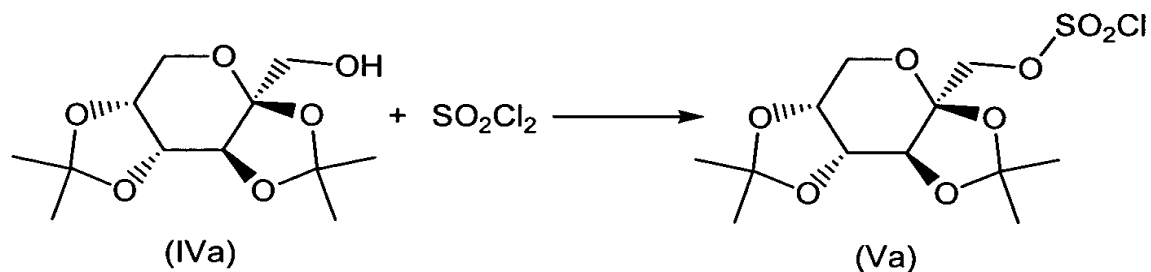
20 24. A pharmaceutical composition made by mixing a pharmaceutically acceptable carrier and the compound of Claim 22.

25 25. A process for making a pharmaceutical composition comprising mixing a pharmaceutically acceptable carrier and the compound of Claim 22.

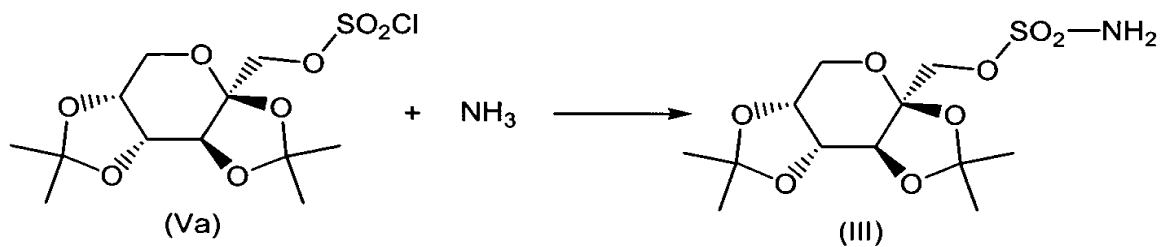
26. A continuous process for the preparation of a compound of formula (III)



comprising



5 (Aa) reacting a compound of formula (IVa) with
sulfuryl chloride;
in the presence of an organic or inorganic base;
in a first organic solvent comprising at least one
solvent selected from a cyclic ether, a straight or
10 branched chain dialkyl ether, an aromatic hydrocarbon,
or a mixture of a cyclic, straight or branched chain
dialkyl ether and an aromatic hydrocarbon solvent;
to form the corresponding compound of formula (Va);



(Ba) reacting the compound of formula (Va) with
ammonia;
in a second organic solvent comprising at least the
20 solvent used in step (A);

to form the corresponding compound of formula (III).

27. The process as in Claim 26, wherein the organic or
5 inorganic base is an organic base.

28. The process as in Claim 27, wherein the organic
base is pyridine.

10 29. The process as in Claim 26, wherein the first
organic solvent comprises at least one solvent selected
from the group consisting of a cyclic ether, a straight
or branched chain dialkyl ether, an aromatic hydrocarbon
solvent and a mixture of a cyclic, straight or branched
15 chain dialkyl ether and an aromatic hydrocarbon solvent.

30. The process as in Claim 29, wherein the first
organic solvent comprises a cyclic ether or a straight
or branched chain dialkyl ether.

20 31. The process as in Claim 30, wherein the first
organic solvent is glyme.

32. The process as in Claim 26 wherein the sulfuryl
25 chloride is present in an amount greater than about 0.9
moles per mole of the compound of formula (IVa).

33. The process as in Claim 26, wherein the base is
present in an amount greater than about 1 molar
30 equivalent of the compound of formula (IVa).

34. The process as in Claim 33, wherein the molar ratio of the compound of formula (IVa) to the base is at least about 1:1.05.

5 35. The process as in Claim 26, wherein the temperature of the reaction in Step (Aa) is less than about 50°C.

36. The process as in Claim 26, wherein the second organic solvent is glyme.

10 37. The process as in Claim 26, wherein the ammonia is present in an amount greater than about 1 molar equivalent of the compound of formula (Va).

15 38. The process as in Claim 37, wherein the molar ratio of the ammonia to the compound of formula (Va) is at least about 2:1.

20 39. The process as in Claim 26, wherein ammonia is fed into the reactor at a pressure of about 19 psia.

40. The process as in Claim 26, wherein the temperature of the reaction in Step (Ba) is in the range of from about -30 to about 50°C.

25 41. The process as in Claim 26, wherein the compound of formula (Va) is formed in a solution comprising the compound of formula (Va) and the first organic solvent.

30 42. The process as in Claim 41, wherein the sulfonyl chloride is reacted in amount equal to about 1 equivalent relative to the compound of formula (IVa), further comprising concentrating the solution comprising

the compound of formula (Va) and the first organic solvent to remove at least about 20% of the solvent mass.

5 43. The process as in Claim 41, wherein the sulfuryl chloride is reacted in amount greater than about 1 equivalent relative to the compound of formula (IVa), further comprising concentrating the solution comprising the compound of formula (Va) and the first organic
10 solvent to remove at least 70% of the solvent mass.

44. The process as in Claim 41, further comprising concentrating the solution comprising the compound of formula (Va) and the first organic solvent to an oil.

15 45. The process as in Claim 41, further comprising treating the solution comprising the compound of formula (Va) and the first organic solvent to remove volatiles.

20 46. The process as in Claim 26, wherein step (Bb) is run in a continuous stirred tank reactor.

47. The process as in Claim 26, wherein step (Aa) and step (Ba) are each run in a continuous stirred tank reactor.

25 48. A compound prepared according to the process of Claim 26.

30 49. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the compound of Claim 48.

50. A pharmaceutical composition made by mixing a pharmaceutically acceptable carrier and the compound of Claim 48.

- 5 51. A process for making a pharmaceutical composition comprising mixing a pharmaceutically acceptable carrier and the compound of Claim 48.